ACCESS DB # 164659

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Sabiha Qazi Examiner # : 74141 Date: 8/31/05

Art Unit: 1616 Phone Number: 2-0622 Serial Number: ~~10~~ 09/928,890

Location (Bldg/Room#): 4A45 (Mailbox #): 04C70 Results Format Preferred (circle): PAPER DISK

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MY

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Method of treatment of cancer by controlling graft-Versus-Leukemia using topical active corticosteroids

Inventors (please provide full names): McDonald et al.

Earliest Priority Date: 8/13/2001.

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Please search for the method of treating a human patient with cancer by an steroid beclomethasone 17,21-dipropionate to reduce the mortality associated GVHD (Graft-v-Host Disease) as in Cl 1.

Please see Cls 7+ 15 where this compd is used in combination of other drugs additionally

You may search Medline, Biosis and Caplus.

Please see attached sheets.

Thank you.

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=> d his ful

     (FILE 'HOME' ENTERED AT 17:06:53 ON 14 SEP 2005)

     FILE 'HCAPLUS' ENTERED AT 17:07:09 ON 14 SEP 2005
                E MCDONALD GEORGE B/AU
L1           38 SEA ABB=ON  "MCDONALD GEORGE B"/AU
                E STERGIOPOULOS NICHOLAS/AU
L2            4 SEA ABB=ON  "STERGIOPOULOS NICHOLAS"/AU
L3            2 SEA ABB=ON  L1 AND L2
L4              ANALYZE L3 1-2 CT :       15 TERMS

     FILE 'REGISTRY' ENTERED AT 17:33:22 ON 14 SEP 2005
L5            5 SEA ABB=ON  (PREDNISONE OR PREDNISOLONE OR CYCLOSPORINE OR
                METHOTREXATE OR TACROLIMUS)/CN
                E ANTI-LYMPHOCYTE GLOBULIN/CN
                E GLOBULIN ANTI-LYMPHOCYTE/CN
                E GLOBULIN, ANTI-LYMPHOCYTE/CN
                E ANTI-T-CELL MONOCLONAL ANTIBODIES/CN
L6            1 SEA ABB=ON  BECLOMETHASONE 17,21-DIPROPIONATE/CN

     FILE 'HCAPLUS' ENTERED AT 17:35:00 ON 14 SEP 2005
L7         1030 SEA ABB=ON  (?HEMATOPOIETIC?(3W)?CELL?(3A)?TRANSPLANT)
L8          173 SEA ABB=ON  L7 AND (?GVHD? OR ?GRAFT?(W)V(W)?HOST?(W)?DISEASE?)
L9            1 SEA ABB=ON  L8 AND GVL(W)?REACT?
L10          67 SEA ABB=ON  L8 AND (?CANCER? OR ?CARCIN? OR ?NEOPLASM? OR
                ?TUMOR? OR ?TUMOUR?)
L11           1 SEA ABB=ON  L10 AND (L6 OR ?BECLOMETHASONE-17,21-DIPROPIONAT?)
L12          26 SEA ABB=ON  L10 AND (L5 OR ?PREDNISONE? OR ?PREDNISOLONE? OR
                ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI?(W)?LYMPHOCYTE?(W)?GLO
                BULIN? OR ?ANTI?(W)T(W)?CELL?(W)(MONOCLONAL?(W)?ANTIBOD? OR
                ?IMMUNOTOXIN?))
L13          26 SEA ABB=ON  L11 OR L12
L14           6 SEA ABB=ON  L13 AND (PRD<20010813 OR PD<20010813)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
     17:42:24 ON 14 SEP 2005
L15          24 SEA ABB=ON  L13
L16          16 DUP REMOV L15 (8 DUPLICATES REMOVED)

     FILE 'USPATFULL' ENTERED AT 17:46:17 ON 14 SEP 2005
L17          15 SEA ABB=ON  L13 AND (PRD<20010813 OR PD<20010813)
L18           0 SEA ABB=ON  L17 AND (L6 OR ?BECLOMETHASONE?-17,21-?DIPROPIONAT?
                )

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
     17:47:18 ON 14 SEP 2005
L19           0 SEA ABB=ON  L16 AND (L6 OR ?BECLOMETHASONE-17,21-DIPROPIONAT?)


     FILE 'HCAPLUS' ENTERED AT 17:48:02 ON 14 SEP 2005
L20           1 SEA ABB=ON  L10 AND ?BECLOMETHASONE?

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
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L21           0 SEA ABB=ON  L16 AND ?BECLOMETHASONE?

     FILE 'USPATFULL' ENTERED AT 17:48:46 ON 14 SEP 2005
L22           0 SEA ABB=ON  L17 AND ?BECLOMETHASONE?
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Same strategy for online search"

6 cits from CA Plus

16 cits from above db's

15 cits from USPatFull

FILE HOME

FILE HCAPLUS

FILE COVERS 1907 - 14 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 13 Sep 2005 (20050913/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2
DICTIONARY FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE MEDLINE
FILE LAST UPDATED: 14 SEP 2005 (20050914/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 8 September 2005 (20050908/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 9 Sep 2005 (20050909/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 5 SEP 2005 <20050905/UP>
FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 13 SEP 2005 (20050913/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Sep 2005 (20050913/PD)
FILE LAST UPDATED: 13 Sep 2005 (20050913/ED)
HIGHEST GRANTED PATENT NUMBER: US6944881
HIGHEST APPLICATION PUBLICATION NUMBER: US2005198721

CA INDEXING IS CURRENT THROUGH 13 Sep 2005 (20050913/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Sep 2005 (20050913/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

Inventor Search

=> d ibib abs ind l3 1-2

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:118593 HCAPLUS
DOCUMENT NUMBER: 138:148132
TITLE: Method of treatment of cancer by controlling graft-versus-leukemia using topical active corticosteroids
INVENTOR(S): **McDonald, George B.**; **Stergiopoulos, Nicholas**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

This is the only cit I could locate with beclomethasone-17,21-dipropionate. It dropped out of regular search because of more recent date.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003032631	A1	20030213	US 2001-928890	20010813
PRIORITY APPLN. INFO.:			US 2001-928890	20010813

AB A method for the improved treatment of blood-borne cancers, such as lymphomas, leukemia, and myeloma is disclosed. The method comprises the oral administration of an effective amount of a topically active corticosteroid (TAC) to a patient who has undergone hematopoietic cell transplantation. Administration of the TAC controls a graft-vs.-leukemia (GVL) reaction that is induced following a hematopoietic cell transplantation, so that a GVHD reaction does not develop, or is reduced in severity. The GVL reaction effects killing of cancerous tumor cells in the blood, mediated by the cells derived from the hematopoietic cell transplantation.

IC ICM A61K031-56
INCL 514178000; 514179000; 514180000
CC 2-4 (Mammalian Hormones)
ST leukemia treatment cancer corticosteroid host versus graft allotransplant
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte globulins, in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)
IT Neoplasm
(blood-born; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)
IT Transplant and Transplantation
(graft-vs.-host reaction, prevention and reduction of symptoms; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)
IT Transplant and Transplantation
(hematopoietic cells; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)
IT T cell (lymphocyte)
(immunotoxins and antibodies against; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)
IT Drug delivery systems
(immunotoxins, anti-T-cells, in combination with corticosteroids;

methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Antitumor agents
Human
Leukemia
Lymphoma
Multiple myeloma
(methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, anti-T-cells, in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT 50-24-8, Prednisolone 53-03-2, Prednisone 59-05-2, Methotrexate 59865-13-3, Cyclosporine 104987-11-3, Tacrolimus
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT 76-25-5 1524-88-5, Flurandrenolide 3093-35-4, Halcinonide 3385-03-3, Flunisolide 5534-09-8, Beclomethasone 17,21-dipropionate 5534-18-9, Beclomethasone-17-monopropionate 25122-46-7, Clobetasol propionate 33564-31-7, Diflorasone diacetate 51333-22-3, Budesonide 51372-28-2 51372-29-3 66734-13-2, Alclometasone dipropionate 66852-54-8, Halobetasol propionate 80474-14-2, Fluticasone propionate 83919-23-7, Mometasone furoate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:505407 HCAPLUS
DOCUMENT NUMBER: 137:42096
TITLE: Method of long-term treatment of graft-versus-host disease using topical active corticosteroids
INVENTOR(S): **McDonald, George B.; Stergiopoulos, Nicholas**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002086857	A1	20020704	US 2001-753814		20010103
US 2004006053	A1	20040108	US 2003-613788		20030703
PRIORITY APPLN. INFO.:			US 2000-233194P	P	20000915

US 2001-753814 B1 20010103

AB A method for long-term therapy using corticosteroids to treat tissue damage associated with graft-vs.-host disease in a patient having undergone hematopoietic cell transplantation, and host-vs.-graft disease in a patient having undergone organ allograft transplantation. The method includes orally administering to the patient a therapeutically effective amount of a topically active corticosteroid, such as beclomethasone dipropionate, from the 29th day until the 56th day following hematopoietic cell or organ allograft transplantation. Representative tissues includes tissue of the intestine and liver, while representative tissue damage includes inflammation thereof.

IC ICM A61K031-573

INCL 514179000

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 15

ST graft vs host disease treatment corticosteroid

IT Transplant and Transplantation
(allotransplant; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT Transplant and Transplantation
(graft-vs.-host reaction; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT Transplant and Transplantation
(hematopoietic cell transplantation; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT Human
Inflammation
Intestine, disease
Liver, disease
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT Hematopoietic precursor cell
(transplant; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

IT 50-24-8, Prednisolone 53-03-2, Prednisone 76-25-5, Triamcinolone acetonide 1524-88-5, Flurandrenolide 3093-35-4, Halcinonide 3385-03-3, Flunisolide 5534-09-8, Beclomethasone dipropionate 5534-18-9, Beclomethasone-17-monopropionate 25122-46-7, Clobetasol propionate 33564-31-7, Diflorasone diacetate 51333-22-3, Budesonide 51372-28-2 51372-29-3 66734-13-2, Alclometasone dipropionate 66852-54-8, Halobetasol propionate 80474-14-2, Fluticasone propionate 83919-23-7, Mometasone furoate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

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=> d que stat l14
L5          5 SEA FILE=REGISTRY ABB=ON  (PREDNISONE OR PREDNISOLONE OR
              CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
L6          1 SEA FILE=REGISTRY ABB=ON  BECLOMETHASONE 17,21-DIPROPIONATE/CN
L7       1030 SEA FILE=HCAPLUS ABB=ON  (?HEMATOPOIETIC?(3W)?CELL?(3A)?TRANSPL
              ANT)
L8        173 SEA FILE=HCAPLUS ABB=ON  L7 AND (?GVHD? OR ?GRAFT?(W)V(W)?HOST?
              (W)?DISEASE?)
L10        67 SEA FILE=HCAPLUS ABB=ON  L8 AND (?CANCER? OR ?CARCIN? OR
              ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
L11         1 SEA FILE=HCAPLUS ABB=ON  L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
              IPROPIONAT?)
L12        26 SEA FILE=HCAPLUS ABB=ON  L10 AND (L5 OR ?PREDNISONE? OR
              ?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI?(W)?
              LYMPHOCYTE?(W)?GLOBULIN? OR ?ANTI?(W)T(W)?CELL?(W)(MONOCLONAL?(
              W)?ANTIBOD? OR ?IMMUNOTOXIN?))
L13        26 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L14         6 SEA FILE=HCAPLUS ABB=ON  L13 AND (PRD<20010813 OR PD<20010813)

=> d ibib abs l14 1-6

L14  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2001:917046  HCAPLUS
DOCUMENT NUMBER:         136:193827
TITLE:                   Nonablative allogeneic hematopoietic transplantation
                         as adoptive immunotherapy for indolent lymphoma: low
                         incidence of toxicity, acute graft-versus-host
                         disease, and treatment-related mortality
AUTHOR(S):               Khouri, Issa F.; Saliba, Rima M.; Giralt, Sergio A.;
                         Lee, Ming-Sheng; Okoroji, Grace-Julia; Hagemeister,
                         Fredrick B.; Korbling, Martin; Younes, Anas; Ippoliti,
                         Cindy; Gajewski, James L.; McLaughlin, Peter;
                         Anderlini, Paolo; Donato, Michele L.; Cabanillas,
                         Fernando F.; Champlin, Richard E.
CORPORATE SOURCE:        Departments of Blood and Marrow Transplantation,
                         Lymphoma, Laboratory Medicine, University of Texas M.
                         D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE:                  Blood (2001), 98(13), 3595-3599
                         CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER:               American Society of Hematology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   This study investigated the use of a nonablative conditioning regimen to
     decrease toxicity and achieve engraftment of an allogeneic blood stem cell
     transplant, allowing a graft-vs.-malignancy effect to occur. All patients
     had follicular or small cell lymphocytic lymphoma after relapse from a
     prior response to conventional chemotherapy. Patients received a
     preparative regimen of fludarabine (25 mg/m2 given daily for 5 days or 30
     mg/m2 daily for 3 days) and i.v. cyclophosphamide (1 g/m2 given daily for
     2 days or 750 mg/m2 daily for 3 days). Nine patients received rituximab
     in addition to the chemotherapy. Tacrolimus and methotrexate were
     used for graft-vs.-host disease (GVHD) prophylaxis. Twenty
     patients were studied; their median age was 51 yr. Twelve were in
     complete remission (CR) at transplantation. All patients achieved
     engraftment of donor cells. The median number of days with severe
     neutropenia was 6. Only 2 patients required more than one platelet
     transfusion. The cumulative incidence of acute grade II to IV
     GVHD was 20%. Only one patient developed acute GVHD of
     greater than grade II. All patients achieved CR. None have had a relapse
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of disease, with a median follow-up period of 21 mo. The actuarial probability of being alive and in remission at 2 yr was 84% (95% confidence interval, 57%-94%). Nonablative chemotherapy with fludarabine/cyclophosphamide followed by allogeneic stem cell transplantation is a promising therapy for indolent lymphoma with minimal toxicity and myelosuppression. Further studies are warranted to compare nonablative allogeneic hematopoietic transplantation with alternative treatment strategies.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:549793 HCAPLUS
DOCUMENT NUMBER: 135:327107
TITLE: Nonmyeloablative hematopoietic cell transplantation: Replacing high-dose cytotoxic therapy by the graft-versus-**tumor** effect
AUTHOR(S): Feinstein, Lyle; Sandmaier, Brenda; Maloney, David; McSweeney, Peter A.; Maris, Michael; Flowers, Christopher; Radich, Jerry; Little, Marie-Terese; Nash, Richard A.; Chauncey, Thomas; Woolfrey, Ann; Georges, George; Kiem, Hans-Peter; Zaucha, Jan M.; Blume, Karl G.; Shizuru, Judith; Niederwieser, Dietger; Storb, Rainer
CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, WA, 98109-1024, USA
SOURCE: Annals of the New York Academy of Sciences (**2001**), 938(Hematopoietic Stem Cells 2000), 328-339
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conventional allografting produces considerable regimen-related toxicities that generally limit this treatment to patients younger than 55 yr and in otherwise good medical condition. T cell-mediated graft-vs.-**tumor** (GVT) effects are known to play an important role in the elimination of malignant disease after allotransplants. A minimally myelosuppressive regiment that relies on immunosuppression for allogeneic engraftment was developed to reduce toxicities while optimizing GVT effects. Pre-transplant total-body irradiation (200 cGy) followed by post-transplant immunosuppression with **cyclosporine** (CSP) and mycophenolate mofetil (MMF) permitted human leukocyte antigen (HLA)-matched sibling donor hematopoietic cell engraftment in 82% of patients (n = 55) without prior high-dose therapy. The addition of fludarabine (90 mg/M2) facilitated engraftment in all 28 subsequent patients. Overall, fatal progression of underlying disease occurred in 20% of patients after transplant. Non-relapse mortality occurred in 11% of patients. Toxicities were low. Grade 2-4 acute graft-vs.-host disease (**GVHD**) associated with primary engraftment developed in 47% of patients, and was readily controlled in all but two patients. Donor lymphocyte infusions (DLI) were not very effective at converting a low degree of mixed donor/host chimerism to full donor chimerism; however, the addition of fludarabine reduced the need for DLI. With a median follow-up of 244 days, 68% of patients were alive, with 42% of patients in complete remission, including mol. remissions. Remissions occurred gradually over periods of weeks to a year. If long-term efficacy is demonstrated, such a strategy would expand treatment options for patients who would otherwise be excluded from conventional allografting.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:417759 HCAPLUS
DOCUMENT NUMBER: 135:162240
TITLE: Hematopoietic cell transplantation in older patients with hematologic malignancies: replacing high-dose cytotoxic therapy with graft-versus-**tumor** effects
AUTHOR(S): McSweeney, Peter A.; Niederwieser, Dietger; Shizuru, Judith A.; Sandmaier, Brenda M.; Molina, Arthur J.; Maloney, David G.; Chauncey, Thomas R.; Gooley, Theodore A.; Hegenbart, Ute; Nash, Richard A.; Radich, Jerald; Wagner, John L.; Minor, Steven; Appelbaum, Frederick R.; Bensinger, William I.; Bryant, Eileen; Flowers, Mary E. D.; Georges, George E.; Grumet, F. Cart; Kiem, Hans-Peter; Torok-Storb, Beverly; Yu, Cong; Blume, Karl G.; Storb, Rainer F.
CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA
SOURCE: Blood (**2001**), 97(11), 3390-3400
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Toxicities have limited the use of allogeneic hematopoietic cell transplantation (HCT) to younger, medically fit patients. In a canine HCT model, a combination of postgrafting mycophenolate mofetil (MMF) and **cyclosporine** (CSP) allowed stable allogeneic engraftment after minimally toxic conditioning with low-dose (200 cGy) total-body irradiation (TBI). These findings, together with the known **antitumor** effects of donor leukocyte infusions (DLIs), led to the design of this trial. Forty-five patients (median age 56 yr) with hematol. malignancies, HLA-identical sibling donors, and relative contraindications to conventional HCT were treated. Immunosuppression involved TBI of 200 cGy before and CSP/MMF after HCT. DLIs were given after HCT for persistent malignancy, mixed chimerism, or both, Regimen toxicities and myelosuppression were mild, allowing 53% of eligible patients to have entirely outpatient transplantations. Nonfatal graft rejection occurred in 20% of patients. Grades II to III acute graft-vs.-host disease (**GVHD**) occurred in 47% of patients with sustained engraftment. With median follow-up of 417 days, survival was 66.7%, nonrelapse mortality 6.7%, and relapse mortality 26.7%. Fifty-three percent of patients with sustained engraftment were in complete remission, including 8 with mol. remissions. This novel allografting approach, based on the use of post-grafting immunosuppression to control graft rejection and **GVHD**, has dramatically reduced the acute toxicities of allografting. HCT with the induction of potent graft-vs.-**tumor** effects can be performed in previously ineligible patients, largely in an outpatient setting. Future protocol modifications should reduce rejection and **GVHD**, thereby facilitating studies of allogeneic immunotherapy for a variety of malignancies.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:427885 HCAPLUS
DOCUMENT NUMBER: 131:97039

TITLE: A new preconditioning regimen with melphalan, busulphan and total body irradiation followed by low-dose immunosuppressant in allogeneic hemopoietic stem cell transplantation
AUTHOR(S): Murata, Makoto; Nishida, Tetsuya; Haneda, Masataka; Kanie, Tadaharu; Taji, Hirofumi; Iida, Hiroatsu; Suzuki, Ritsuro; Hamaguchi, Motohiro; Minami, Saburo; Kodera, Yoshihisa
CORPORATE SOURCE: Department of Internal Medicine, Japanese Red Cross Nagoya First Hospital, Nagoya, 453-8511, Japan
SOURCE: British Journal of Haematology (**1999**), 105(3), 799-802
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty adult patients with high-risk leukemia underwent allogeneic hemopoietic stem cell transplantation after melphalan, busulfan and total body irradiation followed by short-term **methotrexate** and low-dose **cyclosporine** or tacrolimus. Three patients developed veno-occlusive disease and no patient developed renal dysfunction. Seven patients experienced grade II-IV acute graft-vs.-host disease (**aGVHD**) and five patients experienced grade III-IV. The 3-yr probabilities of relapse and leukemia-free survival were 22±11% (95% confidence interval) and 50±11%, resp. These data suggest that this preconditioning regimen followed by a low-dose immunosuppressant provided a more anti-leukemic effect without increased regimen-related toxicity and **aGVHD.**
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:409973 HCAPLUS
DOCUMENT NUMBER: 131:82719
TITLE: Total body irradiation, thiotepa, and cyclophosphamide as a conditioning regimen for children with acute lymphoblastic leukemia in first or second remission undergoing bone marrow transplantation with HLA-identical siblings
AUTHOR(S): Zecca, Marco; Pession, Andrea; Messina, Chiara; Bonetti, Federico; Favre, Claudio; Prete, Arcangelo; Cesaro, Simone; Porta, Fulvio; Mazzarino, Ida; Giorgiani, Giovanna; Rondelli, Roberto; Locatelli, Franco
CORPORATE SOURCE: Department of Pediatrics, University of Pavia, IRCCS Policlinico San Matteo, Pavia, I-27100, Italy
SOURCE: Journal of Clinical Oncology (**1999**), 17(6), 1838-1846
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: Allogeneic hematopoietic stem-cell transplantation (HSCT) from HLA-identical siblings can be used to treat children with acute lymphoblastic leukemia (ALL). However, a significant proportion of patients with ALL who undergo HSCT relapse. For this reason, we prospectively evaluated a preparative regimen that included total body irradiation (TBI), thiotepa (TT), and cyclophosphamide (CY) in patients with high-risk ALL in first complete remission (CR) and in children with ALL in

second CR. Patients and Methods: Forty children (median age, 9 yr; range, 1 to 18 yr) with ALL in first or second CR who underwent allogeneic HSCT from HLA-identical siblings were conditioned with a combination of fractionated TBI, TT (10 mg/kg), and CY (120 mg/kg over 2 days). Graft-vs.-host disease (**GVHD**) prophylaxis consisted of **cyclosporine** administered i.v. at a dose of 1 to 3 mg/kg/d for the first 21 days and subsequently orally at a dose of 6 mg/kg/d. Results: All assessable patients were engrafted, with a median time of 11 and 24 days for neutrophil and platelet recovery, resp. The preparative regimen was well tolerated. Only one patient died as a result of regimen-related causes. Eight patients relapsed at a median time of 8 mo after transplantation (range, 3 to 9 mo), and this determined a cumulative probability of relapse of 23%. Twenty-six of 40 patients (65%) are alive and in complete hematol. remission, with a median observation time of 36 mo (range, 14 to 57 mo), which results in a disease-free survival (DFS) at 3 yr of 65%. The 13 patients who underwent transplantation in first CR had a DFS of 85%, whereas the 27 patients who underwent HSCT in second CR had a DFS of 56%. Conclusion: These data suggest that TT is an effective cytotoxic drug that can be safely added to the classical TBI-CY regimen. Because of its cell cycle-independent action, good CNS diffusion, and limited extramedullary toxicity, TT may contribute to increasing the percentage of children with ALL who are successfully cured with allogeneic BMT.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:344857 HCAPLUS
DOCUMENT NUMBER: 131:4246
TITLE: Treatment of hematologic disorders
INVENTOR(S): Sykes, Megan; Spitzer, Thomas R.
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925367	A2	19990527	WO 1998-US24209	19981113 <--
WO 9925367	A3	19990805		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309919	AA	19990527	CA 1998-2309919	19981113 <--
EP 1030675	A2	20000830	EP 1998-960199	19981113 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001523645	T2	20011127	JP 2000-520800	19981113 <--
US 2001048921	A1	20011206	US 1998-191970	19981113 <--
US 6558662	B2	20030506		
US 2003157077	A1	20030821	US 2003-374302	20030225 <--

PRIORITY APPLN. INFO.: US 1997-73230P P 19971114 <--
US 1998-191970 A1 19981113 <--
WO 1998-US24209 W 19981113 <--

AB The inventors have discovered that hematol. disorders, e.g., both neoplastic (hematol. **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-vs.-leukemia (GVL) effect and the like. The method comprises administration of myeloreductive treatment (such as immunosuppressant regimen), introduction of allogeneic donor hematopoietic stem cell to form chimeric bone marrow in the recipient, and an immunosuppressant regimen after donor stem cell introduction to prevent graft-vs.-host response. The immunosuppressant regimen includes depletion of host T lymphocytes and/or NK cells by treating with anti-CD4 or CD8 antibodies, anti-thymocyte globulin, anti-lymphoblast globulin, thymic irradiation, and cytoreductive agents (e.g. alkylating agents, alkyl sulfonates, nitrosoureas, triazenes, antimetabolites, pyrimidine or purine analogs, vinca alkaloids, epipodophyllotoxins, antibiotics, and others).

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=> d que stat l16
L5            5 SEA FILE=REGISTRY ABB=ON  (PREDNISONE OR PREDNISOLONE OR
                CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
L6            1 SEA FILE=REGISTRY ABB=ON  BECLOMETHASONE 17,21-DIPROPIONATE/CN
L7         1030 SEA FILE=HCAPLUS ABB=ON  (?HEMATOPOIETIC?(3W)?CELL?(3A)?TRANSPL
                ANT)
L8          173 SEA FILE=HCAPLUS ABB=ON  L7 AND (?GVHD? OR ?GRAFT?(W)V(W)?HOST?
                (W)?DISEASE?)
L10          67 SEA FILE=HCAPLUS ABB=ON  L8 AND (?CANCER? OR ?CARCIN? OR
                ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
L11           1 SEA FILE=HCAPLUS ABB=ON  L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
                IPROPIONAT?)
L12          26 SEA FILE=HCAPLUS ABB=ON  L10 AND (L5 OR ?PREDNISONE? OR
                ?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI?(W)?
                LYMPHOCYTE?(W)?GLOBULIN? OR ?ANTI?(W)T(W)?CELL?(W)(MONOCLONAL?(
                W)?ANTIBOD? OR ?IMMUNOTOXIN?))
L13          26 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L15          24 SEA L13
L16          16 DUP REMOV L15 (8 DUPLICATES REMOVED)

=> d ibib abs l16 1-16

L16  ANSWER 1 OF 16  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ACCESSION NUMBER:   2005209012  EMBASE
TITLE:              Allogeneic hematopoietic cell transplantation for infants
                    with acute lymphoblastic leukemia.
AUTHOR:             Sanders J.E.; Im H.J.; Hoffmeister P.A.; Gooley T.A.;
                    Woolfrey A.E.; Carpenter P.A.; Andrews R.G.; Bryant E.M.;
                    Appelbaum F.R.
CORPORATE SOURCE:   J.E. Sanders, Fred Hutchinson Cancer Res. Center, Clinical
                    Research Division, 1100 Fairview Ave N, Seattle, WA 98109,
                    United States. jsanders@fhcrc.org
SOURCE:             Blood, (1 May 2005) Vol. 105, No. 9, pp. 3749-3756.
                    Refs: 48
                    ISSN: 0006-4971  CODEN: BLOOAW
COUNTRY:            United States
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       025     Hematology
LANGUAGE:           English
SUMMARY LANGUAGE:   English
ENTRY DATE:         Entered STN: 20050602
                    Last Updated on STN: 20050602
AB   The role of transplantation in infants with acute lymphoblastic leukemia
     (ALL) is not defined. We analyzed results of 40 infants diagnosed before
     age 12 months who received a hematopoietic cell
     transplant (HCT) between July 1982 and February 2003 in first
     complete remission (CR1; n = 17), CR2/3 (n = 7), or relapse (n = 16).
     Patients were conditioned with cyclophosphamide with total body
     irradiation (n = 39) or busulfan (n = 1). Donors were matched related (n
     = 8), mismatched related (n = 16), or un-related (n = 16).
     Graft-versus-host disease (GVHD) prophylaxis was
     methotrexate or cyclosporine (n = 7) or
     methotrexate plus cyclosporine (n = 33). Thirty-nine
     patients engrafted, 20 developed acute GVHD, and 7 developed
     chronic GVHD. Sixteen patients relapsed and 7 died of other
     causes. Patients in CR1 had disease-free survival (DFS) of 76% compared
     with 45% for CR2/CR3 and 8% for relapse (P < .001). Of 33 patients with
     cytogenetic data, 26 (79%) had MLL gene rearrangement. Fourteen of these
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26 were in CR1 and 11 survive in remission. Outcome was associated with phase of disease, but having the MLL gene was not a factor predictive of outcome. Late effects included growth and other hormone deficiencies. These data demonstrate that infants with ALL and MLL gene have excellent DFS when they received transplants in CR1, and consideration for transplantation in CR1 is warranted. .COPYRGT. 2005 by The American Society of Hematology.

L16 ANSWER 2 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2004635617 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15610251
TITLE: Acute renal failure after myeloablative **hematopoietic cell transplant**: incidence and risk factors.
AUTHOR: Hingorani Sangeeta R; Guthrie Katherine; Batchelder Ami; Schoch Gary; Aboulhosn Nada; Manchion Janel; McDonald George B
CORPORATE SOURCE: Department of Pediatrics and Medicine, University of Washington, Seattle, Washington, USA.. sangeeta.hingorani@seattlechildrens.org
CONTRACT NUMBER: CA15704 (NCI)
CA18029 (NCI)
K23 DK 63038 (NIDDK)
SOURCE: Kidney international, (2005 Jan) 67 (1) 272-7. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20041222
Last Updated on STN: 20050622
Entered Medline: 20050621

AB BACKGROUND: Survival after myeloablative therapy followed by **hematopoietic cell transplant** (HCT) is limited by substantial treatment-related toxicities. Acute renal failure (ARF) develops in 25% to 50% of patients after HCT. METHODS: One hundred forty-seven patients were followed prospectively from time of transplant. ARF was defined as a doubling of baseline serum creatinine at any time during the first 100 days post-transplant. We conducted a nested case-control study to identify precipitants of ARF. For each person who developed ARF, 2 controls were selected at random from patients who had not developed ARF as of that time. An exposure period was defined for each case as the 2 weeks prior to the day on which the matched case met the criteria for ARF. The risk of ARF in relation to demographic and anthropometric characteristics, and to types of treatment and comorbidity, was examined using univariable and multivariable conditional logistic regression models. Odds ratios for the associations with ARF were estimated, taking into account the matching. RESULTS: Fifty-three patients (36%) developed ARF at a median of 33 days after transplant (range 1 to 97). Elevated risks were observed in patients who received liposomal amphotericin (OR 6.58; 95%CI 1.45-29.95) and conventional (OR 3.60; 95%CI 0.79-16.55), and in those patients with sinusoidal obstruction syndrome (SOS) (previously termed veno-occlusive disease) (OR 9.37; 95%CI 2.29-38.38). For every 0.1 mg/dL increase in baseline serum Cr, the risk of ARF decreased by 30%. Neither total body irradiation (TBI) dose, levels of metabolites of cyclophosphamide, sepsis, acute graft versus host disease (**GVHD**), nor **cyclosporine** (CSA) levels was associated with an increased risk of ARF. CONCLUSION: The cumulative

incidence of ARF after HCT remains high. Amphotericin use during the 2-week exposure period and presence of hepatic sinuosoidal injury increased the risk of ARF within the first 100 days after HCT. Higher levels of serum creatinine at baseline were associated with a lower risk of ARF.

L16 ANSWER 3 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005322961 EMBASE
TITLE: Risk factors for bronchiolitis obliterans in allogeneic hematopoietic stem-cell transplantation for leukemia.
AUTHOR: Santo Tomas L.H.; Loberiza Jr. F.R.; Klein J.P.; Layde P.M.; Lipchik R.J.; Rizzo J.D.; Bredeson C.N.; Horowitz M.M.
CORPORATE SOURCE: Dr. L.H. Santo Tomas, Division of Pulmonary and Critical Care Medicine, Medical College of Wisconsin, 9200 West Wisconsin Ave, Milwaukee, WI 53226, United States. santo@mcw.edu
SOURCE: Chest, (2005) Vol. 128, No. 1, pp. 153-161.
Refs: 62
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
017 Public Health, Social Medicine and Epidemiology
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050818
Last Updated on STN: 20050818

AB Study objectives: Reported risk factors for bronchiolitis obliterans (BO) in allogeneic **hematopoietic** stem-**cell transplant** recipients come from modest-sized studies and are limited to experiences of single institutions. We sought to identify risk factors for BO using data from the International Bone Marrow Transplant Registry. Methods: Registry data on 6,275 adult patients with leukemia who received human leukocyte antigen-identical sibling transplants from 1989 to 1997 and survived at least 100 days after transplantation were evaluated for the study. Risk factors for BO were analyzed using proportional hazards regression. Results: Seventy-six patients were found to have BO, with an incidence rate of 1.7% at 2 years after transplantation. The Kaplan-Meier estimate of median time to onset of BO was 431 days. Histologic evaluation was performed in 36 patients (47%). In 28 patients (37%), diagnosis was based on pulmonary function tests, CT scans of the chest, or a combination of both. On multivariate analysis, the factors that were associated with an increased risk for BO included the following: peripheral blood-derived stem cell, a busulfan-based conditioning regimen, interval from diagnosis to transplant ≥ 14 months, female donor to male recipient sex match, prior interstitial pneumonitis, and an episode of moderate-to-severe acute graft-vs-host disease (**GVHD**). Conclusion: In addition to corroborating previously reported risk factors, such as acute **GVHD** and a busulfan-based conditioning regimen, we found that peripheral blood stem-cell transplantation, long duration to transplant, female donor to male recipient, and a prior episode of interstitial pneumonitis are associated with an increased risk for BO.

L16 ANSWER 4 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2005060091 EMBASE
TITLE: Outcomes of transplantation with partial T-cell depletion of matched or mismatched unrelated or partially matched related donor bone marrow in children and adolescents with leukemias.
AUTHOR: Bunin N.; Aplenc R.; Leahey A.; Magira E.; Grupp S.; Pierson G.; Monos D.
CORPORATE SOURCE: Dr. N. Bunin, Division of Oncology, Children's Hospital of Philadelphia, 34th and Civic Center Blvd., Philadelphia, PA 19104, United States. buninn@email.chop.edu
SOURCE: Bone Marrow Transplantation, (2005) Vol. 35, No. 2, pp. 151-158.
Refs: 31
ISSN: 0268-3369 CODEN: BMTRE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050218
Last Updated on STN: 20050218

AB Graft-versus-host disease (**GVHD**) remains a major barrier to successful **hematopoietic** stem **cell transplant** for patients who lack a matched related donor. Partial T-cell depletion (TCD) of the graft may decrease the risk of severe **GVHD** with unrelated donors (URD) and partially matched related donors (PMRD) while retaining an antileukemic effect. We analyzed our experience using URD and PMRD for pediatric patients with leukemias from 1990 to 2001. A subgroup of 'matched' URD donor pairs was retrospectively analyzed for high-resolution class I. Partial TCD was accomplished with monoclonal antibody T10B9 or OKT3 and complement. There were 76 URD (45% matched) and 28 PMRD recipients. Event-free survival (EFS) was 38.3%, and overall survival (OS) 45.1% at 3 years. On multivariate analysis, there was no difference in survival based upon marrow source, but nonrelapse mortality was higher with the use of PMRD. Relapse occurred in 6% of ALL patients, and 22.8% of AML/MDS patients. Grades III-IV **GVHD** was observed in only 6.7% of patients. Partial TCD allows use of matched or mismatched URD, or PMRD with little mortality from **GVHD**, durable engraftment, and no increase in relapse risk. .COPYRGT. 2005 Nature Publishing Group All rights reserved.

L16 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004201882 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14990986
TITLE: A novel reduced intensity regimen for allogeneic hematopoietic stem cell transplantation associated with a reduced incidence of graft-versus-host disease.
AUTHOR: Miller K B; Roberts T F; Chan G; Schenkein D P; Lawrence D; Sprague K; Gorgun G; Relias V; Grodman H; Mahajan A; Foss F M
CORPORATE SOURCE: Department of Medicine, Bone Marrow Transplantation and Hematological Malignancy Unit, Beth Israel Deaconess

Medical Center, Boston, MA 02215, USA..
kbmiller@BIDMC.harvard.edu
SOURCE: Bone marrow transplantation, (2004 May) 33 (9) 881-9.
Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040422
Last Updated on STN: 20041219
Entered Medline: 20041119

AB Summary:In all, 55 patients at high risk or ineligible for a conventional allogeneic **hematopoietic** stem **cell transplant** (HSCT) received a regimen consisting of extracorporeal photopheresis, pentostatin, and reduced dose total body irradiation. The median age was 49 years (18-70 years); 44 received a sibling and 11 an unrelated HSCT; 44% were over the age of 50 years and 31% had undergone a prior HSCT. Graft-versus-host disease (**GVHD**) prophylaxis consisted of **cyclosporine** and **methotrexate.** Full donor chimerism was documented in 98% by day +100. The 1000-day nonrelapse mortality was 11%. The median follow-up is 502 days (154-1104 days). The 1- and 2-year overall survival (OS) and event-free survival (EFS) are 67, 58 and 55%, and 47%, respectively. Patients who had not received a prior HSCT or had less than three prior chemotherapy regimens had a 71% OS and 67% EFS at 1 year. Greater than grade II **aGVHD** developed in 9% and chronic **GVHD** (**cGVHD**) in 43%, and extensive in 12% and limited in 31%. Of the patients, 86% who engrafted had a disease response, 72% had complete and 14% partial responses. This novel reduced intensity preparative regimen was well tolerated and associated with a low incidence of transplant-related mortality and serious acute and **cGVHD.**

L16 ANSWER 6 OF 16 EMBASE
on STN

ACCESSION NUMBER: 2004517300 EMBASE
TITLE: Differential diagnosis of cholestasis following allogeneic hematopoietic stem cell transplantation in children: The contribution of serum bile acid levels in relation to other liver function tests.
AUTHOR: Zakrzewski J.L.; Ballauff A.; Wieland R.; Basu O.; Kremens B.
CORPORATE SOURCE: Dr. B. Kremens, University Hospitals of Essen, Dept. of Pediat. Hematol., Oncol./E., Hufelandstr. 55, 45122 Essen, Germany. bernhard.kremens@uni-essen.de
SOURCE: Pediatric Hematology and Oncology, (2004) Vol. 21, No. 8, pp. 697-705.
Refs: 16
ISSN: 0888-0018 CODEN: PHONEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
007 Pediatrics and Pediatric Surgery
025 Hematology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041228

Last Updated on STN: 20041228

AB Hepatic complications associated with cholestasis occur frequently in **hematopoietic** stem **cell transplant** recipients. Since bile acid seems to be a sensitive indicator of beginning cholestasis, the authors monitored total serum bile acid levels in addition to the standard liver function tests in 23 recipients of allogeneic transplants between June 1999 and September 2000. The observations suggest that bile acid is an early and sensitive marker of hepatic **GvHD** but not as specific as bilirubin. For cholestasis in absence of hepatic **GvHD** bile acid seems to be more sensitive than bilirubin. Routinely monitoring of bile acid after hematopoietic stem cell transplantation is not indicated.

L16 ANSWER 7 OF 16 EMBASE on STN

ACCESSION NUMBER: 2003413766 EMBASE

TITLE: Infliximab use in patients with severe graft-versus-host disease and other emerging risk factors of non-Candida invasive fungal infections in allogeneic **hematopoietic** stem **cell transplant** recipients: A cohort study.

AUTHOR: Marty F.M.; Lee S.J.; Fahey M.M.; Alyea E.P.; Soiffer R.J.; Antin J.H.; Baden L.R.

CORPORATE SOURCE: F.M. Marty, Brigham and Women's Hospital, Division of Infectious Diseases, PBB-A4, 75 Francis St, Boston, MA 02115, United States. fmarty@partners.org

SOURCE: Blood, (15 Oct 2003) Vol. 102, No. 8, pp. 2768-2776. Refs: 45
ISSN: 0006-4971 CODEN: BLOOAW

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20031106
Last Updated on STN: 20031106

AB Acute graft-versus-host disease (**GVHD**) is a common complication of allogeneic hematopoietic stem cell transplantation (HSCT). It has been proposed that **tumor** necrosis factor α (TNF-α) blockade with infliximab may be an effective treatment for severe (grades III-IV) **GVHD.** We determined it infliximab use in this high-risk population was associated with an additional increased risk of non-Candida invasive fungal infections (IFIs). Records of the 2000-2001 HSCT cohort at our institution were reviewed. Fifty-three (20%) of 264 evaluable patients developed severe **GVHD** and 11 of these 53 (21%) received infliximab for treatment. Proven or probable IFI was documented in 10 (19%) of 53 patients with severe **GVHD** (incidence rate of 0.99 cases/1000 **GVHD** patient-days). When stratified by infliximab use, 5 of 11 infliximab recipients developed an IFI (6.78 cases/1000 **GVHD** patient-days), compared with 5 of 42 IFI cases among nonrecipients (0.53 cases/1000 **GVHD** patient-days). In a time-dependent Cox regression model among patients with severe **GVHD**, the adjusted IFI hazard ratio of infliximab exposure was 13.6 (P = .004; 95% CI, 2.29-80.2). We conclude that infliximab administration is associated with a significantly increased risk of

non-Candida IFI in HSCT recipients with severe **GVHD** disease. Pre-emptive systemic antifungal therapy against molds should be considered in patients who develop severe **GVHD** after HSCT if infliximab is used. .COPYRGT. 2003 by The American Society of Hematology.

L16 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:152543 BIOSIS
DOCUMENT NUMBER: PREV200400147930
TITLE: Reduced intensity conditioning regimen (RIC) with CD 45 monoclonal antibodies for stem cell transplantation using matched unrelated (MUD) or mismatched donors.
AUTHOR(S): Popat, Uday [Reprint Author]; Carrum, George [Reprint Author]; Kuehnle, Ingrid [Reprint Author]; Bollard, Catherine; Gottschalk, Stephen; Heslop, Helen [Reprint Author]; Krance, Robert; Brenner, Malcolm [Reprint Author]
CORPORATE SOURCE: Department of Medicine, Baylor College of Medicine, Houston, TX, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 705a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB **Hematopoietic** stem **cell transplant** using RIC decreases morbidity and mortality thereby allowing it to be offered to patients who are otherwise not candidates for allogeneic blood stem cell transplants, because of age or co-morbidity. For optimal **antitumor** effect, complete donor chimerism is likely necessary. Unfortunately, many current conditioning regimens result in mixed chimerism or in graft rejection, and may require post transplant manipulations, such as reduction of immunosuppression that increase the risks of severe **GvHD.** Based on a successful murine model, we have investigated whether CD45 monoclonal antibody (MAb) can deplete recipient immune and hematopoietic cells and facilitate donor engraftment in subablative transplantation of matched unrelated or mismatched unrelated or family donor stem cells. We used two rat anti CD45 monoclonal antibodies against non overlapping epitopes on the CD 45 molecules at a dose of 400 mcg/kg/dayX4 added to our standard RIC regimen of TBI 450 cGY, Fludarabine 120mg/m2, and Campath 1H (30 mg), and FK506 as **GvHD** prophylaxis. 12 patients with hematological malignancies, not eligible for standard transplant because of age or co-morbidities have been enrolled to date. Reasons for reduced intensity transplant included age >55(6 pts), second transplant (5 pts.), Previous fungal infection (2pts.); and abnormal liver (3 pts), kidney (3 pts), cardiac (2 pts) or pulmonary function (3 pts). Median age is 42 yrs (range 1-65 yrs). 7 patients were male, 5 female. 5 patients had MDS or AML, 3 ALL, 2 HD, 1CLL/AA, and 1 NHL. 6 patients were in relapse with active disease and 6 were in complete remission (4 CR1, 2 CR2) at the time of transplant. 9 patients or donors were CMV positive. 5 donors were HLA identical (6/6) but unrelated and 7 donors had one antigen mismatch. (5 unrelated, 2 family). All but one patient received peripheral blood stem cells. All 12 patients engrafted. Median time to neutrophil engraftment was 12 days (8-18). By day 30 all the patients were 100% donor chimera, including all

7 patients who had one antigen mismatched (5/6) donors and the 3 patients who had rejected a previous transplant. 1 patient had grade III-IV severe **GvHD**, and 1 had grade II **GvHD.** 1 patient died of progressive disease. 11 patients are alive (10 disease free) 29-279 days (median 116 days) post transplant. We compared the engraftment data with 16 patients (10 MUD, 6 Mismatched donor-5/6) treated on our previous protocol using the same conditioning regimen without CD 45 MAb. 4 of 16 patients rejected their graft compared to none of the patients in current study. Of the 6 donors in this earlier series who received mismatched grafts, 3 rejected, compared to 0/7 following the addition of CD45 MAbs (p=0.07, two tailed Fisher exact test). We are continuing further accrual on this study to determine if this trend to improved engraftment continues. These data suggest that the addition of CD45 MAb to subablative conditioning regimens is safe, may contribute to establishment of complete donor chimerism, and may be of particular value when transplantation uses HLA mismatched donor stem cells.

L16 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003490760 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14569561
TITLE: Reduced-intensity allogeneic stem cell transplantation for patients whose prior autologous stem cell transplantation for hematologic malignancy failed.
AUTHOR: Fung H C; Cohen S; Rodriguez R; Smith D; Krishnan A; Somlo G; Sahebi F; Senitzer D; O'Donnell M R; Stein A; Snyder D S; Spielberger R; Bhatia R; Falk P; Molina A; Nademanee A; Parker P; Kogut N; Popplewell L; Vora N; Margolin K; Forman S J
CORPORATE SOURCE: Division of Hematology and Bone Marrow Transplantation, Kaiser Permanente-City of Hope BMT Program, City of Hope Cancer Center, 1500 E. Duarte Road, Duarte, CA 91010, USA.. hfung@coh.org
CONTRACT NUMBER: CA 33572 (NCI)
P01 CA 30206 (NCI)
SOURCE: Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, (2003 Oct) 9 (10) 649-56.
Journal code: 9600628. ISSN: 1083-8791.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20031022
Last Updated on STN: 20040625
Entered Medline: 20040624

AB Autologous hematopoietic stem cell transplantation (autoSCT) is an effective treatment for patients with various hematologic malignancies. Despite the significant improvement in the overall outcome, disease progression after transplantation remains the major cause of treatment failure. With longer follow-up, therapy-related myelodysplasia/acute myelogenous leukemia is becoming an important cause of treatment failure. The prognosis for these 2 groups of patients is very poor. Allogeneic hematopoietic stem cell transplantation (alloSCT) is a potential curative treatment for these patients. However, the outcome with conventional myeloablative alloSCT after failed autoSCT is typically poor because of high transplant-related mortality. In an attempt to reduce the treatment-related toxicity, we studied a reduced-intensity conditioning

regimen followed by alloSCT for patients with progressive disease or therapy-related myelodysplasia/acute myelogenous leukemia after autoSCT. This report describes the outcomes of 28 patients with hematologic malignancies who received a reduced-intensity alloSCT after having treatment failure with a conventional autoSCT. Fourteen patients received a **hematopoietic** stem **cell transplant** from a related donor and 14 from an unrelated donor. The conditioning regimen consisted of low-dose (2 Gy) total body irradiation with or without fludarabine in 4 patients and the combination of melphalan (140 mg/m(2)) and fludarabine in 24. **Cyclosporine** and mycophenolate mofetil were used for posttransplantation immunosuppressive therapy, as well as graft-versus-host disease (**GVHD**) prophylaxis, in all patients. All patients engrafted and had >90% donor chimerism on day 100 after SCT. Currently, 13 patients (46%) are alive and disease free, 7 patients (25%) developed disease progression after alloSCT, and 8 (32%) died of nonrelapse causes. Day 100 mortality and nonrelapse mortality were 25% and 21%, respectively. With a median follow-up of 24 months for surviving patients, the 2-year probabilities of overall survival, event-free survival, and relapse rates were 56.5%, 41%, and 41.9%, respectively. Six patients (21%) developed grade III to IV acute **GVHD.** Among 21 evaluable patients, 15 (67%) developed chronic **GVHD.** We conclude that (1) reduced-intensity alloSCT is feasible and has an acceptable toxicity profile in patients who have previously received autoSCT and that (2) although follow-up was short, a durable remission may be achieved in some patients who would otherwise be expected to have a poor outcome.

L16 ANSWER 10 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:181399 BIOSIS
DOCUMENT NUMBER: PREV200400181250
TITLE: Risk factors for severe graft-versus-host disease after nonmyeloablative hematopoietic cell transplantation for treatment of hematological malignancies.
AUTHOR(S): Flowers, Mary E. D. [Reprint Author]; Traina, Fabiola [Reprint Author]; Storer, Barry [Reprint Author]; Maris, Michael [Reprint Author]; Bethge, Wolfgang [Reprint Author]; Carpenter, Paul [Reprint Author]; Maloney, David [Reprint Author]; Storb, Rainer [Reprint Author]; Sandmaier, Brenda M. [Reprint Author]; Martin, Paul J. [Reprint Author]
CORPORATE SOURCE: Clinical Research Division, Department of Medicine, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 152a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

AB The efficacy of nonmyeloablative allogeneic **hematopoietic cell transplant** (HCT) depends on the balance between beneficial antineoplastic effects weighed against detrimental effects related to graft-versus-host disease (**GVHD**). Risk factors for

severe, life-threatening **GVHD** were analyzed retrospectively among 171 consecutive patients who had related or unrelated nonmyeloablative HCT for treatment of hematologic malignancies. The conditioning regimen was 2.0 Gy total body irradiation with or without fludarabine, and mycophenolate mofetil and **cyclosporine** were used for post-transplant immunosuppression. Overall, 44 of 171 (26%) patients developed severe **GVHD** with a median follow-up of 30 (range, 12-65) months. The incidence of severe **GVHD** was similar after related and unrelated HCT. Manipulation of immunosuppression to induce graft-versus-leukemia/**tumor** effects in patients with relapsing/persistent disease was not associated with subsequent development of severe **GVHD** (P=0.98). In a Cox regression analysis, factors that were significantly associated with severe, life-threatening **GVHD** were: diagnosis of myeloid malignancies (P=.01), donor lymphocyte infusion for persistent, progressive or recurrent malignancy (P=.05) and, preceding non-severe acute **GVHD** (P=.002). The cumulative incidence of severe **GVHD** at 2 years after HCT was 37% among patients with myeloid malignancies, compared to 21% among those with non-myeloid malignancies. Nonrelapse mortality at 3 years after transplant was 33% for patients with myeloid malignancies and 24% for those with non-myeloid malignancies (P=0.20). We speculate that the increased risk of severe **GVHD** among patients with myeloid diseases could be related to the antigen-presenting function of malignant myeloid cells. The differences in risk of severe, life-threatening **GVHD** according to myeloid or non-myeloid disease category should be taken into account in the design of future clinical trials.

L16 ANSWER 11 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:337177 BIOSIS
DOCUMENT NUMBER: PREV200300337177
TITLE: Infectious Complications in Long-Term Survivors of Cord Blood Stem Cell Transplantation (CBSCT); Experience at Roswell Park **Cancer** Institute.
AUTHOR(S): Alam, Arif R. [Reprint Author]; Varma, Geetha; Hahn, Theresa; Segal, Brahm; Paplham, Pamela; Becker, Joanne; Baer, Maria; Bambach, Barbara; Silva, Joaquin; Slack, James; Wetzler, Meir; McCarthy, Philip L. Jr.
CORPORATE SOURCE: Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2479. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

AB Umbilical cord blood is a source of stem cells for patients undergoing unrelated **hematopoietic** stem **cell transplant** . The recipients are at an increased risk of infectious complications because of slower engraftment kinetics in the acute period post-CBSCT; however, there is no long term data regarding infectious complications post day 100. We investigated the infectious complications in our long-term survivors (LTS) after CBSCT. Between 5/97 and 10/2001, 26 patients received a CBSCT for a hematologic malignancy. 11 patients died before day 100 of infection (n=4), regimen-related toxicity (n=4),

GVHD (n=1), recurrent disease (n=1) and graft failure (n=1) and were excluded from this analysis. In the 15 long-term survivors, median age at CBSCT was 34 years (range 5-53 years). Donor-recipient HLA match was 6/6 (n=1), 5/6 (n=6), or 4/6 (n=8). Seven patients had sex mismatched CB donors. **AGVHD** prophylaxis was **Cyclosporine** (CsA), **Methylprednisolone** (MP) regimen (n=12), or CsA, MP and ATG (n=3). CsA was changed to FK506 in 7 patients due to CsA toxicity. Median nucleated cell dose was 2.25 (range, 0.134-0.423) x 107/kg and median CD34+ cell dose was 0.115 (range, 0.025-0.191) x 106/kg). Median time to ANC>500/mm3 was 34 days (range, 16-104) and median time to platelet count >20,000/mm3 was 66 days (range, 41-144). Median follow-up post CBSCT in the long-term survivors was 33.7 months (range 5.4 - 47.1). 5 of the 15 LTS developed chronic graft-versus-host disease (**cGVHD**) (limited n=1, extensive n=4). 6 of the 15 LTS developed opportunistic infections (herpes zoster n=1, disseminated invasive aspergillosis n=2, localized pulmonary aspergillosis n=1, disseminated candida glabrata n=1, pulmonary atypical mycobacterium infection n=1). 3 of the 6 patients with opportunistic infections have died of refractory leukemia (n=1), relapsed leukemia (n=1) or multi-organ failure due to infection (n=1). The remaining patients were either successfully treated (resection of localized pulmonary aspergillosis n=1) or are currently receiving active treatment for fungal disease n=2, and atypical mycobacterium n=1. At the time of this report, 4 of the 15 LTS have died. Patients post CBSCT remain at risk for opportunistic infections. This risk appears to be increased in patients who develop **cGVHD** and require immunosuppression. Selected patients may benefit from more aggressive anti-microbial prophylaxis to prevent opportunistic infections during immunosuppressive therapy.

L16 ANSWER 12 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:336363 BIOSIS
DOCUMENT NUMBER: PREV200300336363
TITLE: Kinetics of Mixed Chimerism in Peripheral Blood Hematopoietic Subpopulations from 120 Patients after Nonmyeloablative **Hematopoietic** Stem **Cell Transplant.**
AUTHOR(S): Little, Marie-Terese [Reprint Author]; Baker, Jennifer E. [Reprint Author]; Sandmaier, Brenda M. [Reprint Author]; Maris, Michael B. [Reprint Author]; Maloney, David [Reprint Author]; Gooley, Theodore [Reprint Author]; Oparin, Dmitrij [Reprint Author]; Zellmer, Eustacia [Reprint Author]; Mielcarek, Marco [Reprint Author]; Wagner, John [Reprint Author]; Shizuru, Judith [Reprint Author]; Blume, Karl [Reprint Author]; Chauncey, Thomas [Reprint Author]; Storb, Rainer [Reprint Author]
CORPORATE SOURCE: Clinical Research Division, Fred Hutchinson Cancer Research CTR, Seattle, WA, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 136. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB The kinetics of donor engraftment in peripheral blood hematopoietic subpopulations from 120 patients (median age 54 years) undergoing nonmyeloablative hematopoietic stem cell transplantation (HSCT) were analyzed. The nonmyeloablative approach consisted of total body irradiation (200 cGy), marrow (n=10) or PBSC (n=110) allografts, and postgrafting immunosuppression with mycophenolate mofetil and **cyclosporine.** Sixty-two percent of the patients received fludarabine (30mg/m2 on days -4, -3, -2) before HSCT. Patients received either HLA matched related (n=87) or unrelated donor (n=33) HSCT for cervical **cancer** (n=1) or hematologic malignancies (n=119) including ALL (n=2), AML (n=17), CLL (n=13), CML (n=14), HD (n=11), MDS (n=19), MM (n=24), NHL (n=19). Graft rejection or failure occurred in 12/120 (10%) of patients. Acute **GVHD** of grades II and III-IV occurred in 41% and 13% of patients, respectively. Peripheral blood samples were sorted on post-transplant days 14, 28, 42, 56, 84, 180 and 365 by multidimensional FACS into CD3+CD56- (T-lymphocytes), CD3+CD4+CD8- (CD4+ T-lymphocytes), CD3+CD4-CD8+ (CD8+ T-lymphocytes) CD45+side scatter mid-hi (granulocytes), CD56+CD3- (NK cells), and CD14+CD3-CD56-(monocytes) fractions. Percentages of donor chimerism were analyzed by PCR-based VNTR analyses and quantified by phosphoimage analyses. On day 14 post-transplant, the highest degree of donor reconstitution was noted in the NK fraction followed by CD8+ T-lymphocytes, CD3+ lymphocytes, CD4+ T-lymphocytes, monocytes, and granulocytes. On day 28, donor granulocyte chimerism rapidly increased, followed by progressive increases in the remaining cell populations. Most patients remained mixed donor/host chimeras for extended periods of time (at least to 180 days post-transplant) with greater than 60% donor chimerism in each subpopulation. This pattern of donor reconstitution was consistent for all of the patients with hematologic malignancies except those with CML and MDS where percentages of donor T-lymphocyte chimerisms were lower. Patients receiving PBSC product had a higher degree of donor T lymphocyte chimerism than recipients of marrow (p=.02). Greater intensity of therapy before HSCT was associated with higher degrees of donor granulocyte, CD3+ lymphocyte, and monocyte chimerisms. The association of donor chimerism with survival and progression-free survival was assessed by Cox regression analysis, and donor chimerism was treated as a time-dependent covariate. A high degree of donor NK cell chimerism was consistently associated with improved overall survival and progression-free survival (p=.02 and .002, respectively). The CD4/CD8 absolute cell ratio was consistently >1 immediately after transplant in the 38 patients that were analyzed. There was no correlation with CD4 donor chimerism nor absolute cell counts and overall survival. There was a suggestion that increased donor CD8 chimerism was associated with decreased risk of mortality before (p=.05) and after (p=.08) adjusting for absolute donor counts in this smaller sample size (n=38). These results suggest that monitoring mixed chimerism early after transplant is important for determining outcomes and for the development of new strategies for intervention.

L16 ANSWER 13 OF 16 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002016110 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11418375
TITLE: Conventional hematopoietic stem cell transplants from identical or alternative donors are feasible in recipients relapsing after an autograft.
AUTHOR: di Grazia C; Raiola A M; Van Lint M T; Lamparelli T; Gualandi F; Berisso G; Bregante S; Dominietto A; Mordini N; Bruno B; Frassoni F; Bacigalupo A
CORPORATE SOURCE: Dipartmento di Ematologia, Ospedale San Martino, Genoa,

Italy.. emato2@smartino.ge.it
SOURCE: Haematologica, (2001 Jun) 86 (6) 646-51.
Journal code: 0417435. ISSN: 0390-6078.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020124
Entered Medline: 20020102

AB BACKGROUND AND OBJECTIVES: The risk of relapse after autologous bone marrow transplantation (ASCT) is high and is related to the type of malignancy and phase of the disease. The outcome for the patient who relapses after an autologous transplant is poor. Some of these patients achieve a remission with conventional chemotherapy, but it is usually short-lasting. Most of them succumb to the original disease. One further therapeutic possibility is an allogeneic transplant which would confer the potential advantage of a graft-versus-leukemia effect in addition to the lack of **tumor** contamination of the graft and to a high-dose intensity conditioning regimen. DESIGN AND METHODS: We have studied the outcome of 31 patients with hematologic malignancies who underwent an allogeneic **hematopoietic** stem **cell transplant** (HSCT) after failing an autologous transplant because of relapse (n=29) or persistent aplasia (n=2). The median age at allograft was 36 years (18-55) and the interval from autograft to allograft was 21 months (3-141). The source of stem-cells was unmanipulated bone marrow (n=26) or growth-factor-mobilized peripheral blood (n=5). The donor was an HLA-identical sibling (n=7), or an alternative donor (n=24) (family mismatched n=11, or matched unrelated n=13). The conditioning regimen was cyclophosphamide and thiotepa (n=22), or cyclophosphamide and total body irradiation (n=9) Graft-versus-host disease (**GvHD**) prophylaxis consisted of **cyclosporine** (CyA) + **methotrexate** (MTX). RESULTS: Acute **GvHD** was scored as 0-I, II, or III-IV in 39%, 48%, and 13% of the patients, respectively. Sixteen patients died of transplant-related complications and one of progressive disease. With a median follow-up of 220 days (9-2104) the actuarial 2-year transplant-related mortality (TRM) was 51%, the actuarial relapse risk 37%, the actuarial survival 46%. Fifteen patients (48%) are alive in complete remission, with a median follow-up of 32 months (range 2-71). INTERPRETATION AND CONCLUSIONS: These data suggest that patients relapsing after an autotransplant should be screened for potential related or unrelated donors: although TRM remains high there is a definite chance of long-term disease-free survival if these patients are allografted.

L16 ANSWER 14 OF 16 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001559681 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11607768
TITLE: Fludarabine and melphalan-based conditioning for patients with advanced hematological malignancies relapsing after a previous **hematopoietic** stem **cell transplant.**
AUTHOR: Devine S M; Sanborn R; Jessop E; Stock W; Huml M; Peace D; Wickrema A; Yassine M; Amin K; Thomason D; Chen Y H; Devine H; Maningo M; van Besien K
CORPORATE SOURCE: Stem Cell Transplant Program, University of Illinois College of Medicine, Chicago, IL 60612, USA.
SOURCE: Bone marrow transplantation, (2001 Sep) 28 (6) 557-62.

Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20020802
Entered Medline: 20020801

AB Severe regimen-related toxicity often complicates second transplant procedures performed in patients with hematological malignancies that have relapsed after an initial **hematopoietic** stem **cell** (HSC) **transplant.** Therefore, we studied the safety and efficacy of a reduced-intensity fludarabine and melphalan based conditioning regimen in 11 patients who had relapsed following an autologous (n = 7) or allogeneic (n = 4) HSC transplant. All patients received allogeneic peripheral blood HSC from either an HLA-identical (n = 7) or an HLA-mismatched (n = 4) relative. Diagnoses included AML (n = 9), ALL (n = 1), or Hodgkin's disease (n = 1). Only one patient was in complete remission at the time of second transplant. The median interval between first transplant and relapse was 163 days (range 58-1885). Recipients of HLA-mismatched transplants received antithymocyte globulin in addition to fludarabine and melphalan as part of the conditioning regimen. All 11 patients received acute **GVHD** prophylaxis consisting of tacrolimus and **methotrexate.** Ten of 11 patients achieved hematopoietic engraftment with a median time to absolute neutrophil count >0.5 x 10(9)/l and to platelet count of >20 x 10(9)/l of 14 and 19 days, respectively. All engrafting patients achieved 100% donor chimerism on initial analysis, except for one with persistent leukemia at day +19. Two patients experienced grade 3 regimen-related toxicity, manifesting as acute renal failure. Acute **GVHD** grades 2-4 occurred in two recipients and chronic **GVHD** in four. The 100-day mortality from all causes was 36%. Ten of 11 patients (91%) died a median of 140 days (range 9-996) after the second transplant. The causes of death included relapse (n = 5), sepsis (n = 4), and idiopathic pneumonia syndrome (n = 1). One patient with AML survives in remission at 880 days post-transplant. We conclude that fludarabine- and melphalan-based conditioning promotes full donor chimerism, even following HLA-mismatched transplants. However, the regimen may be more beneficial when applied to patients undergoing allogeneic HSC transplantation earlier in their disease course.

L16 ANSWER 15 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:241260 BIOSIS
DOCUMENT NUMBER: PREV200200241260
TITLE: Analysis of mixed chimerism in peripheral blood hematopoietic subpopulations from 101 patients after nonmyeloablative **hematopoietic** stem **cell** **transplant.**
AUTHOR(S): Little, Marie-Terese [Reprint author]; Baker, Jennifer [Reprint author]; Sandmaier, Brenda [Reprint author]; Maris, Michael [Reprint author]; Maloney, David [Reprint author]; Gooley, Theodore [Reprint author]; Zellmer, Eustacia [Reprint author]; Heimfeld, Shelly [Reprint author]; Georges, George [Reprint author]; Wagner, John [Reprint author]; Shizuru, Judith; Blume, Karl; Chauncey, Thomas [Reprint author]; Storb, Rainer [Reprint author]

CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, WA, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 477a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002

AB Nonmyeloablative hematopoietic stem cell transplantation (HSCT) promotes initial mixed chimerism with limited toxicity. Although the induction of chimerism after allogeneic HSCT has been documented, the kinetics of donor engraftment in different hematopoietic subpopulations as they relate to outcomes have not been extensively studied. Analysis of mixed chimerism was performed in a cohort of 101 patients (median age 54 years) who received either matched related (n=74) or unrelated donor (n=27) nonmyeloablative allogeneic HSCT for a solid **tumor** (n=1) and hematologic malignancies (n=100) including ALL (n=1), AML (n=10), CLL (n=11), CML (n=11), HD (n=11), MDS (n=18), MM (n=24), NHL (n=14). The nonmyeloablative HSCT approach consisted of total body irradiation (200 cGy), bone marrow (n=8) or PBSC (n=93) grafts, and postgrafting immunosuppression with mycophenolate mofetil and **cyclosporine.** In addition, 62% of the patients received fludarabine (30 mg/m2 on days -4, -3, -2). Graft rejection or failure occurred in 10% of patients. Acute **GVHD** of grades II-IV and III-IV occurred in 52% and 15% of patients, respectively (56% and 15% for nonrejectors). Peripheral blood samples were sorted on post-transplant days 14, 28, 42, 56, 84, 180 and 365 by multidimensional FACS into CD3+CD56- (T-lymphocytes), CD45+side scattermid-hi (granulocytes), CD56+CD3- (NK cells), and CD14+CD3-CD56-(monocytes) fractions. Percent donor chimerism was analyzed by PCR-based VNTR analysis and quantified by phosphoimage analysis. Cox regression was used to assess the association of donor chimerism with time-to-event outcomes, survival and relapse-free survival. Donor chimerism was treated as a time-dependent covariate in these models. The hazard of mortality was significantly decreased as percent donor granulocyte chimerism increased. If chimerism was modeled as a continuous variable, an increase of 20% chimerism was associated with a decrease in the hazard of mortality of .77 (hazard ratio (HR)=0.77; 95% CI, 0.60 to 0.98; p=.03). Similarly, as the percent donor NK cell and monocyte chimerism increased, the hazard of mortality decreased (HR=0.75; 95% CI, 0.58 to 0.98; p=.03 and HR=0.70; 95% CI, 0.53 to 0.89 p=.004, respectively). Increasing percent donor T-lymphocyte chimerism was associated with a decrease in hazard of mortality but this association was not statistically significant (p=0.38). There were statistically significant associations between high percentages of donor granulocyte, NK and monocyte chimerisms and increased relapse-free survival (p=.005, .0009 and .03, respectively) and a trend towards an association for increased percent donor T-lymphocyte chimerism (p=.14). Logistic regression was used to assess the association of donor chimerism with the probability of grades II-IV **GVHD**, where the last chimerism value before day 28 and before occurrence of **GVHD** was used as a covariate. There was no statistically significant association between the probability of grades II-IV acute **GVHD** and donor chimerism in any of the sorted subpopulations. The evaluation of early donor chimerism maybe a valuable tool for assessing the risk of mortality and relapse-free survival.

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ACCESSION NUMBER: 2001198963 EMBASE
TITLE: Unrelated cord blood transplant experience by the pediatric blood and marrow transplant consortium.
AUTHOR: Yu L.C.; Wall D.A.; Sandler E.; Chan K.W.; Grayson G.; Kletzel M.
CORPORATE SOURCE: Dr. L.C. Yu, Children's Hospital, 200 Henry Clay Avenue, New Orleans, LA 70118, United States. lyu@lsuhsc.edu
SOURCE: Pediatric Hematology and Oncology, (2001) Vol. 18, No. 4, pp. 235-245.
Refs: 25
ISSN: 0888-0018 CODEN: PHONEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010628
Last Updated on STN: 20010628

AB Cord blood (CB) has emerged as a potential source of hematopoietic stem cells for patients who are in need of **hematopoietic** stem **cell transplant** (HSCT). The authors analyzed the Pediatric Blood and Marrow Transplant Consortium's (PBMTC) data of consecutive unrelated CB transplants performed during the initial 2 years of using placental blood grafts. From January 1995 to December 1996 PBMTC performed a total of 44 unrelated CB transplant for a variety of diseases consisting of acute leukemias (n = 29), congenital conditions (n = 9), and bone marrow failure (n = 6). There were 15 females and 29 males with median age of 5 years (range 0. 4-20.6 years) and median weight of 18.2 kg (range 6.3-70 kg). The median volume of CB units was 80 mL (range 44.5-215 mL) and the median cell dose given was 4.3 x 10(7)/kg of recipient weight (range 1.1-23 x 10(7)/kg). Techniques used for human leukocyte antigen (HLA) matching were serologic typing for class I HLA antigens and high-resolution molecular typing for HLA-DRB(1) alleles. HLA disparities were as follows: 4 were 6/6 matches, 21 were 5/6, 15 were 4/6, and 4 were 3/6. Twenty-nine (66 %) of CB units were DRB(1) matched with recipients. Conditioning regimens consisted of either total body irradiation containing (n = 31) or chemotherapy only (n = 11) regimens. All but 3 patients receive **cyclosporine** as part of graft vs. host disease (**GvHD**) prophylaxis in combination with either **methotrexate** (MTX) or **methylprednisolone** (Pred). The other 3 patients had FK506 and MTX for **GvHD** prophylaxis. Myeloid engraftment (absolute neutrophil count ≥ 500) occurred at a median of 21 days (range 10-43 days) and platelet ≥ 50,000/mm(3) was noted at a median of 44 days (range 16-102 days). Eight patients died too early (<day +28) for evaluation of engraftment (5 for infection, 2 for multiorgan failure, 1 for toxic epidermolysis). The probability of having grade II-IV acute **GvHD** for all patients was 44 ± 0.7%. The incidence of a **GvHD** is similar for 4/6 and 5/6 antigen when DRB(1) matched, at 47 and 52%, respectively. Chronic **GvHD** was noted in 28% of patients surviving > 90 days. The Kaplan-Meir estimate of 4-year event-free survival was 43%. A Cox model for analysis of factors associated with survival was DRB(1) matching, p = .001; cell dose, p = .009; and younger age, p = .03. In conclusion, CB transplant offers a good alternative to bone marrow transplant Although **GvHD** occurs, it is usually of low severity despite the high frequency of multiple HLA

antigen mismatches. It also appears that a 4/6 is as good as a 5/6 matched antigen CB unit when DRB(1) matched especially in the pediatric setting.

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=> d que stat l17
L5            5 SEA FILE=REGISTRY ABB=ON  (PREDNISONE OR PREDNISOLONE OR
                CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
L6            1 SEA FILE=REGISTRY ABB=ON  BECLOMETHASONE 17,21-DIPROPIONATE/CN
L7         1030 SEA FILE=HCAPLUS ABB=ON  (?HEMATOPOIETIC?(3W)?CELL?(3A)?TRANSPL
                ANT)
L8          173 SEA FILE=HCAPLUS ABB=ON  L7 AND (?GVHD? OR ?GRAFT?(W)V(W)?HOST?
                (W)?DISEASE?)
L10          67 SEA FILE=HCAPLUS ABB=ON  L8 AND (?CANCER? OR ?CARCIN? OR
                ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
L11           1 SEA FILE=HCAPLUS ABB=ON  L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
                IPROPIONAT?)
L12          26 SEA FILE=HCAPLUS ABB=ON  L10 AND (L5 OR ?PREDNISONE? OR
                ?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI?(W)?
                LYMPHOCYTE?(W)?GLOBULIN? OR ?ANTI?(W)T(W)?CELL?(W)(MONOCLONAL?(
                W)?ANTIBOD? OR ?IMMUNOTOXIN?))
L13          26 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L17          15 SEA FILE=USPATFULL ABB=ON  L13 AND (PRD<20010813 OR PD<20010813
                )

=> d ibib abs l17 1-15

L17  ANSWER 1 OF 15  USPATFULL on STN
ACCESSION NUMBER:        2005:137498  USPATFULL
TITLE:                   Cellular compositions which facilitate engraftment of
                         hematopoietic stem cells while minimizing the risk of
                         gvhd
INVENTOR(S):             Ildstad, Suzanne T, Louisville, KY, UNITED STATES

                              NUMBER         KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2005118142      A1   20050602
APPLICATION INFO.:       US 2003-485842     A1   20020801  (10)
                         WO 2002-US24402         20020801

                                NUMBER         DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 2003-60309243   20010801                    <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    FROST BROWN TODD, LLC, 2200 PNC CENTER, 201 E. FIFTH
                         STREET, CINCINNATI, OH, 45202, US
NUMBER OF CLAIMS:        36
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      8 Drawing Page(s)
LINE COUNT:              2126
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The present invention provides for cellular compositions which
       facilitate engraftment of hematopoietic stem cells from a syngeneic,
       allogeneic or xenogeneic donor. The cellular compositions of the
       invention facilitate engraftment while minimizing the risk of graft
       versus host disease in the graft recipient. According to a preferred
       embodiment of the invention, a cell composition is provided, which cell
       composition comprises hematopoietic stem cells, such as CD34.sup.+ cells
       and/or facilitating cells, in combination with αβ TCR.sup.+ T
       cells. The invention also relates to methods of using the cellular
       compositions of the invention to induce donor specific tolerance in a
       recipient, thus allowing the transplantation of donor organs, cells and
       tissues. Also disclosed are methods of treating leukemia and
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cancer as well as infectious diseases caused by viruses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 2 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2004:313909 USPATFULL
TITLE: Mixed chimerism and tolerance
INVENTOR(S): Sykes, Megan, Charlestown, MA, UNITED STATES
PATENT ASSIGNEE(S): The General Hospital Corporation, a Massachusetts corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004247579	A1	20041209
	US 6877514	B2	20050412
APPLICATION INFO.:	US 2003-696127	A1	20031029 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2002-155878, filed on 24 May 2002, GRANTED, Pat. No. US 6718986 Division of Ser. No. US 1999-374498, filed on 13 Aug 1999, GRANTED, Pat. No. US 6412492 Division of Ser. No. US 1997-855705, filed on 8 May 1997, GRANTED, Pat. No. US 6006752

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1916
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of inducing tolerance without whole body irradiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 3 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2004:150954 USPATFULL
TITLE: Methods for treating disorders of neuronal deficiency with bone marrow-derived cells
INVENTOR(S): Blau, Helen M., Menlo Park, CA, UNITED STATES
Brazelton, Timothy, Cupertino, CA, UNITED STATES
Weimann, James M., Palo Alto, CA, UNITED STATES
PATENT ASSIGNEE(S): The Board of Trustees of the Leland, Palo Alto, CA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004115175	A1	20040617
APPLICATION INFO.:	US 2003-688747	A1	20031016 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-993045, filed on 13 Nov 2001, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-247128P	20001110 (60)	<--

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 2455
AB The invention provides, among other things, novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of bone marrow derived neurons, whether formed de novo or as a result of fusion with an existing neuron, thereby replacing or repairing lost or damaged neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

L17 ANSWER 4 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2004:88251 USPATFULL
TITLE: Blockade of T cell migration into epithelial **GVHD** target tissues as an approach to achieving anti-**tumor** effects against lymphohematopoietic malignancies without **GVHD**
INVENTOR(S): Sykes, Megan, Charlestown, MA, UNITED STATES
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, 02110 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004067220	A1	20040408
APPLICATION INFO.:	US 2003-437707	A1	20030514 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2001-US43797, filed on 14 Nov 2001, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-248332P	20001114 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 2079
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antagonists of T cell migration are used to reduce **GVHD** in recipients of hematopoietic cell grafts. The administration of antagonists of T cell migration can be used in combination with conventional methods of bone marrow transplantation and in combination with the administration of donor leukocytes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 5 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2003:225266 USPATFULL
TITLE: Treatment of hematologic disorders
INVENTOR(S): Sykes, Megan, Boston, MA, UNITED STATES
Spitzer, Thomas R., Andover, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003157077	A1	20030821
APPLICATION INFO.:	US 2003-374302	A1	20030225 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-191970, filed on 13 Nov 1998, GRANTED, Pat. No. US 6558662

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-73230P	19971114 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 2151
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The inventors have discovered that hematologic disorders, e.g., both neoplastic (hematologic **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-versus-leukemia (GVL) effect and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 6 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2003:123081 USPATFULL
TITLE: Transgenic swine & swine cells having human HLA genes
INVENTOR(S): Seebach, Joerg, Boston, MA, United States
Sachs, David H., Newton, MA, United States
DerSimonian, Harout, Wellesley, MA, United States
LeGuern, Christian, Newton, MA, United States
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6558663	B1	20030506
APPLICATION INFO.:	US 1999-457177		19991208 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1996-692843, filed on 2 Aug 1996, now patented, Pat. No. US 6030833

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1995-1900P	19950804 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wehbe' , Anne M.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 2834
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of promoting tolerance and inhibiting NK cell mediated attack in a human recipient to a swine graft are disclosed The methods include introducing into the recipient a swine hematopoietic stem cell which has been transformed with a transgene encoding a human MHC class I protein that inhibits recipient NK cell mediated attack.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 7 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2003:110472 USPATFULL
TITLE: Mixed chimerism and tolerance
INVENTOR(S): Sykes, Megan, Charlestown, MA, UNITED STATES
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, UNITED STATES, 02110 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003075187	A1	20030424
	US 6718986	B2	20040413
APPLICATION INFO.:	US 2002-155878	A1	20020524 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-374498, filed on 13 Aug 1999, GRANTED, Pat. No. US 6412492 Division of Ser. No. US 1997-855705, filed on 8 May 1997, GRANTED, Pat. No. US 6006752

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1953
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of inducing tolerance without whole body irradiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 8 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2002:300807 USPATFULL
TITLE: Methods for treating disorders of neuronal deficiency with bone marrow-derived cells
INVENTOR(S): Brazelton, Timothy R., Cupertino, CA, UNITED STATES
Blau, Helen M., Menlo Park, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002168350	A1	20021114
APPLICATION INFO.:	US 2001-993045	A1	20011113 (9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-247128P	20001110 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO, CA, 94304-1018

NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 1696
AB The invention provides novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of new neurons in the nervous system, thereby replacing lost neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

L17 ANSWER 9 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2002:159528 USPATFULL
TITLE: Mixed chimerism and tolerance
INVENTOR(S): Sykes, Megan, Boston, MA, United States
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6412492	B1	20020702
APPLICATION INFO.:	US 1999-374498		19990813 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-855705, filed on 8 May 1997, now patented, Pat. No. US 6006752

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Isabella, David J.
LEGAL REPRESENTATIVE: Hale and Dorr LLP
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1977
AB A method of inducing tolerance without whole body irradiation.

L17 ANSWER 10 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2001:223705 USPATFULL
TITLE: TREATMENT OF HEMATOLOGIC DISORDERS
INVENTOR(S): SYKES, MEGAN, BOSTON, MA, United States
SPITZER, THOMAS R., ANDOVER, MA, United States
PATENT ASSIGNEE(S): The General Hospital Corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001048921	A1	20011206
	US 6558662	B2	20030506
APPLICATION INFO.:	US 1998-191970	A1	19981113 (9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-73230P	19971114 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY, HOAG & ELIOT, LLP, PATENT GROUP, ONE POST OFFICE

SQUARE, BOSTON, MA, 02109
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 2152
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The inventors have discovered that hematologic disorders, e.g., both neoplastic (hematologic **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-versus-leukemia (GVL) effect and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 11 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2001:194150 USPATFULL
TITLE: L-leucyl-L-leucine methyl ester treatment of donor lypmhocyte infusions in bone marrow transplant patients
INVENTOR(S): Korngold, Robert, Cherry Hill, NJ, United States
Flomenberg, Neal, Cherry Hill, NJ, United States
Hsieh, Michael, Philadelphia, PA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001036664	A1	20011101	
APPLICATION INFO.:	US 2001-803223	A1	20010309	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-188391P	20000310 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: THOMAS JEFFERSON UNIVERSITY, INTELLECTUAL PROPERTY DIVISION, 1020 WALNUT STREET, SUITE 620, PHILADELPHIA, PA, 19107
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 413
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method of inhibiting graft-versus-host disease in allogeneic **hematopoietic** stem **cell transplant** (HSCT) patients by using L-leucyl-L-leucine methyl ester (LLME) to eliminate selective cytotoxic T cells in donor lymphocyte infusions (DLI). LLME has been shown to inhibit **GVHD** in animal models by selectively inducing apoptosis in natural killer cells and cytotoxic T cells. The application of LLME to the human clinical HSCT situation, however, has been hampered by HSC toxicity when unseparated marrow is treated at the concentrations necessary to purge **GVHD**-inducing T cells prior to infusion. In the present invention, this problem is circumvented by the LLME ex vivo treatment of DLI administered following transplantation of T cell-depleted HSC. In this setting, the effects of LLME on HSC contained within the DLI are irrelevant for clinical outcome. In another embodiment, the risk of toxicity to the stem cell population is avoided by ex vivo LLME treatment of donor lymphocytes after separation of CD34.sup.+ stem cells and then co-administration of the LLME-treated

donor CD34.sup.- fraction and the untreated CD34.sup.+ stem cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 12 OF 15 USPATFULL on STN

ACCESSION NUMBER:	2000:24507 USPATFULL			
TITLE:	Transgenic swine and swine cells having human HLA genes			
INVENTOR(S):	Seebach, Joerg, Boston, MA, United States Sachs, David H., Newton, MA, United States DerSimonian, Harout, Wellesley, MA, United States LeGuern, Christian, Newton, MA, United States			
PATENT ASSIGNEE(S):	The General Hospital, MA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6030833		20000229	<--
APPLICATION INFO.:	US 1996-692843		19960802 (8)	
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1995-1900P		19950804 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Saunders, David			
ASSISTANT EXAMINER:	VanderVegt, F. Pierre			
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.			
NUMBER OF CLAIMS:	14			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 1 Drawing Page(s)			
LINE COUNT:	2801			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A genetically engineered swine cell having a transgene encoding a human HLA protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 13 OF 15 USPATFULL on STN

ACCESSION NUMBER:	1999:169148 USPATFULL			
TITLE:	Mixed chimerism and tolerance			
INVENTOR(S):	Sykes, Megan, Boston, MA, United States			
PATENT ASSIGNEE(S):	The General Hospital Corporation, Boston, MA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6006752		19991228	<--
APPLICATION INFO.:	US 1997-855705		19970508 (8)	
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1996-17099P		19960509 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Isabella, David J.			
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.			
NUMBER OF CLAIMS:	53			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)			

LINE COUNT: 2116
AB A method of inducing tolerance without whole body irradiation.

L17 ANSWER 14 OF 15 USPATFULL on STN
ACCESSION NUMBER: 1998:150448 USPATFULL
TITLE: Transplantation and graft-versus-host-disease
INVENTOR(S): Sachs, David H., Newton, MA, United States
Arn, J. Scott, North Andover, MA, United States
Lorf, Thomas, Hardegsen/Gladebeck, Germany, Federal Republic of
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5843425		19981201	<--
APPLICATION INFO.:	US 1995-461693		19950605	(8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-266427, filed on 19 Jun 1994, now patented, Pat. No. US 5614182 Ser. No. Ser. No. US 1992-838595, filed on 19 Feb 1992, now abandoned Ser. No. Ser. No. US 1995-451210, filed on 26 May 1995, now abandoned Ser. No. Ser. No. US 1994-220371, filed on 29 Mar 1994, now abandoned Ser. No. Ser. No. US 1995-458720, filed on 1 Jun 1995 Ser. No. Ser. No. US 1994-243653, filed on 16 May 1994, now patented, Pat. No. US 5658564 Ser. No. Ser. No. US 1993-114072, filed on 30 Aug 1993, now patented, Pat. No. US 5624823 Ser. No. Ser. No. US 1993-150739, filed on 19 Nov 1993, now abandoned And Ser. No. US 1994-212228, filed on 14 Mar 1994, now abandoned , said Ser. No. US -451210 which is a continuation of Ser. No. US -838595
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Chambers, Jasemine C.
ASSISTANT EXAMINER: Hauda, Karen M.
LEGAL REPRESENTATIVE: Louis Meyers, Lahive & Cockfield
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1,3,5
LINE COUNT: 1579
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of preparing swine donor tissue which includes hematopoietic stem cells and T cells for transplantation into a recipient mammal other than a swine. The method includes the swine donor tissue with an antibody which binds the epitope recognized by the mAb 2-6-15 monoclonal antibody. The binding facilitates depletion of T cells about as efficiently or more efficiently than does the mAb 2-6-15 monoclonal antibody and results in about the same or less depletion of stem cells as does the mAb 2-6-15 monoclonal antibody.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 15 OF 15 USPATFULL on STN
ACCESSION NUMBER: 97:36084 USPATFULL
TITLE: DNA encoding procine interleukin-10
INVENTOR(S): Sachs, David H., Newton, MA, United States
Leguern, Christian A., Newton, MA, United States
Sykes, Megan, Charlestown, MA, United States

	Blancho, Gilles JF., Cambridge, MA, United States
PATENT ASSIGNEE(S):	The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5624823		19970429	<--
APPLICATION INFO.:	US 1993-114072		19930830	(8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1991-797555, filed on 22 Nov 1991, now abandoned And a continuation-in-part of Ser. No. US 1992-838595, filed on 19 Feb 1992, now abandoned And a continuation-in-part of Ser. No. US 1993-63171, filed on 17 May 1993, now abandoned And a continuation-in-part of Ser. No. US 1993-62946, filed on 17 May 1993, now abandoned , said Ser. No. US -838595 which is a continuation-in-part of Ser. No. US 1992-817761, filed on 8 Jan 1992, now abandoned , said Ser. No. US -63171 which is a continuation-in-part of Ser. No. US -838595 And Ser. No. US -797555 , said Ser. No. US -62946 which is a continuation-in-part of Ser. No. US -838595

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Walsh, Stephen G.
ASSISTANT EXAMINER:	Kemmerer, Elizabeth C.
LEGAL REPRESENTATIVE:	Myers, Ph.D., LouisLahive & Cockfield
NUMBER OF CLAIMS:	27
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT:	1826

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Purified DNA encoding porcine IL-10, porcine IL-10, and methods of inducing immunological tolerance and inhibiting graft versus host disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.